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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/632,875	08/01/2003	Raymond F. Schinazi	60137.0017USU1	3042

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MERCHANT & GOULD PC
P.O. BOX 2903
MINNEAPOLIS, MN 55402-0903

EXAMINER	
KHARE, DEVESH	
ART UNIT	**PAPER NUMBER**
1623	

DATE MAILED: 10/06/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/632,875	SCHINAZI ET AL.	
	Examiner	Art Unit	
	Devesh Khare	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 July 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-60* is/are pending in the application.

4a) Of the above claim(s) *1-30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *31-60* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Applicant's election of the claims of Group I corresponding to claims 31-60 in the reply filed on 07/31/2006 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-30 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected subject matter.

An action on the merits of claims 31-60 is contained herein below.

Objection

Claims 40 and 42 are objected.

In claims 40 (ii) and 42 (ii), the use of "' " together with ";" is not consistent.

Appropriate correction is required.

Specification

The disclosure is objected to because of the following informalities:

The status of the related application cited at the first page of the specification should be updated to ensure a properly completed file record. This application lacks the necessary reference to 60/453,716 filed 08/01/2002.

Appropriate correction is required.

35 U.S.C. 112, first paragraph rejection

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 31-45 and 58-60 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the HCV polymerase inhibition assay, does not reasonably provide enablement for the prophylaxis of an HCV infection in a host, which comprises the use of an effective treatment amount of a 2',3'-dideoxynucleoside of the formula of claim 31 or a pharmaceutically acceptable salt or prodrug thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

A conclusion of lack of enablement means that, based on the evidence regarding each of the factors below, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation.

The factors regarding undue experimentation have been summarized in *In re Wands,* 858 F.2d 731, 8 USPQ2d 1400 (Fed. Circ. 1988) as follows:

(1) The quantity of experimentation necessary (time and expense);

(2) The amount of direction or guidance presented;

(3) The presence or absence of working examples of the invention;

(4) The nature of the invention;

(5) The state of the prior art;

(6) The predictability or unpredictability of the art;

(7) The breadth of the claims; and

(8) The relative skill of those in the art.

With regard to factors (1) and (2) cited above, undue experimentation is required to determine how an effective treatment amount of a 2',3'-dideoxynucleoside of the formula of claim 31 or a pharmaceutically acceptable salt or prodrug thereof can be used for the prophylaxis of an HCV infection. There has not been provided adequate guidance in the written description for accomplishing such, as only the HCV polymerase assay; BVDV inhibition assay; and cytotoxicity testing of candidate anti-Flaviviridae compounds is disclosed and no prophylaxis of an HCV infection, which comprises an effective treatment amount of a 2',3'-dideoxynucleoside of the formula of claim 31, is described.

With regard to factors (4), (5) and (6), it is noted that there is a great deal of unpredictability in the art. The art at the time the invention was made fails to establish predictability with regard to use of an effective treatment amount of a 2',3'-dideoxynucleoside of the formula of claim 31 or a pharmaceutically acceptable salt or prodrug thereof can be used for the prophylaxis of an HCV infection. The specificity of Hepatitis C virus (HCV) NS3 NTPase and helicase activities with respect to dideoxy-nucleoside triphosphates is disclosed by Locatelli et al. The field related to the

prophylaxis of an HCV infection with an effective treatment amount of a 2',3'-dideoxynucleoside is not well developed, and as such, relatively unpredictable.

With regard to factors (3) and (7), it is noted that while in Examples 11 and 12, pages 53-54 the assays related to HCV polymerase inhibition and BVDV inhibition is disclosed and instant claims are directed to the prophylaxis of an HCV infection, which comprises an effective treatment amount of a 2',3'-dideoxynucleoside of the formula of claim 31 or a pharmaceutically acceptable salt or prodrug thereof, it is not seen as sufficient to support the breath of the claims wherein an effective treatment amount of a 2',3'-dideoxynucleoside of the formula of claim 31 or a pharmaceutically acceptable salt or prodrug thereof can be used for the prophylaxis of an HCV infection.

With regard to factor (8), the relative skill in the art as it relates to the use of an effective treatment amount of a 2',3'-dideoxynucleoside of the formula of claim 31 or a pharmaceutically acceptable salt or prodrug thereof for the prophylaxis of an HCV infection, is that of a Ph.D. or M.D. level.

Presently, the instant specification is not seen to provide an enabling disclosure for the scope of the invention as set forth in instant claims, which encompass use of an effective treatment amount of a 2',3'-dideoxynucleoside of the formula of claim 31 or a pharmaceutically acceptable salt or prodrug thereof for the prophylaxis of an HCV infection in a host. It is noted that Law requires that the disclosure of an application shall inform those skilled in the art how to use applicant's alleged discovery, not how to find out how to use it for themselves, see In re Gardner et al. 166 USPQ 138 (CCPA 1970). In the instant case, the amount of experimentation needed to verify the efficacy of the

prophylaxis of an HCV infection in a host, which comprises the use of an effective treatment amount of a 2',3'-dideoxynucleoside of the formula of claim 31 or a pharmaceutically acceptable salt or prodrug thereof, would indeed be voluminous and unduly burdensome in view of the teachings of the instant disclosure.

35 U.S.C. 112, second paragraph rejection

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 31-38,40,42-45,46-50,52 and 54-60 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(1) Regarding claims 31(i) and 46 (i), the phrase "such as" renders the claim indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

(2) The phrase "capable of" in claims 31(iv); 40(ii); 42(ii); 46(iv); 52(ii) and 54(ii), is a relative term, which renders the claim indefinite. The pharse "capable of" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Claims which depend from an indefinite claim which fail to obviate the indefiniteness of the claim from which they depend are also seen to be indefinite and are also rejected for the reasons set forth supra.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 31-60 are rejected under 35 U.S.C. 102(e) as being anticipated by Mueller et al (Mueller) (US 6,545,021).

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

It is noted that the intended use of the instant composition for the treatment and/or prophylaxis of an HCV infection or for reducing the biological activity of a *Flaviviridae* viral infection does not have any patentable weight towards the claimed composition.

Mueller discloses the pharmaceutical composition of 2',3'-dideoxy-beta-L5-fluorocytidine (beta-L-FddC); 2',3'-dideoxy-beta-L-5-thiacytidine; and 2',3'-dideoxy-beta-L-5-cytidine (beta-L-ddC) (col.64, lines 18-20). Mueller discloses said compounds alone or in combination of other anti-hepatitis virus compounds provide treatment for hepatitis B and C virus infections (col.5, lines 45-50); and Table 1 (cols. 65-68) discloses other antiviral agents such as interferon. The pharmaceutical composition of comprising the

effective amount of said isolated compounds having the pharmaceutical acceptable salts (col.5, lines 50-55); the effective amounts for administration to a mammal (col.6, lines 5-15) and human (col.9, line 40) and a pharmaceutical acceptable carrier (col.6, lines 44-45) is disclosed. Forms of hepatitis such as B, C, delta, E, F and G are disclosed (col.7, lines 5-12). Mueller also discloses that said compounds can exist in the form of optical isomers such as enantiomers because they possess one or more asymmetric carbon (col.60, lines 30-33 and 60-65).

With regard to claims wherein said compounds are used against *Flaviviridae* viral infection, the reference is silent on the use of these compounds, per se. However, the reference discloses that these compounds are useful for the treatment of retroviruses such as HIV and also useful against viruses, including both RNA and DNA viruses (col.2, line 56 to col.3, line 1). It is well known that *Flaviviridae* is a single stranded RNA virus.

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 31-35, 39-42, 46-56 and 58-60 are rejected under 35 U.S.C. 102(b) as being anticipated by Lin et al (Lin) (US 5,627,160).

It is noted that the intended use of the instant composition for the treatment and/or prophylaxis of an HCV infection or for reducing the biological activity of a *Flaviviridae* viral infection does not have any patentable weight towards the claimed composition.

Lin discloses the pharmaceutical composition of 2',3'-dideoxy-beta-L5-fluorocytidine (beta-L-FddC); and 2',3'-dideoxy-beta-L-5-cytidine (beta-L-ddC) (col.5, line 28 and see

the structure in lines 55-65). Mueller discloses said compounds alone or in combination of other anti-hepatitis virus compounds provide treatment for HIV infections (col.13, lines 42-45). The pharmaceutical composition of comprising the effective amount of beta-L-FddC (col.12, lines 5-15); having a pharmaceutical acceptable carrier (col.12, lines 26-50) is disclosed. Lin discloses the administration of said composition to an animal or human patients (col.4, lines 10-20). The prodrugs of said compounds are also disclosed (col.4, lines 25-28 and col.11, lines 51-55).

With regard to claims wherein said compounds are used against an HCV or *Flaviviridae* viral infection, the reference is silent on the use of these compounds, per se. However, the reference discloses that these compounds are useful for the treatment of HBV, HIV and other retroviruses such as HBV (abstract).

Claims 31-35, 39-42 and 46-54 are rejected under 35 U.S.C. 102(b) as being anticipated by Lin et al (Lin) (Biochemical Pharmacology, vol. 47, no.2, pp 171-174, 1994).

It is noted that the intended use of the instant composition for the treatment and/or prophylaxis of an HCV infection or for reducing the biological activity of a *Flaviviridae* viral infection does not have any patentable weight towards the claimed composition. Lin discloses 2',3'-dideoxy-beta-L5-fluorocytidine (beta-L-FddC); and 2',3'-dideoxy-beta-L-5-cytidine (beta-L-ddC) (page 172, 2nd para.). Lin discloses that these compounds were tested in drug susceptibility assays against HIV-1 in MT2 cells in buffer solution (page 172, last para.).

With regard to claims wherein said compounds are used against an HCV or *Flaviviridae* viral infection, the reference is silent on the use of these compounds, per se. However, the reference discloses that these compounds are useful for the treatment of HBV, HIV and other retroviruses such as HBV (abstract).

Claims 31-60 are rejected under 35 U.S.C. 102(b) as being anticipated by Schinazi et al (Schinazi) (US 5,990,093).

It is noted that the intended use of the instant composition for the treatment and/or prophylaxis of an HCV infection or for reducing the biological activity of a *Flaviviridae* viral infection does not have any patentable weight towards the claimed composition.

Schinazi discloses the pharmaceutical composition of 2',3'-dideoxy-beta-L5-fluorocytidine (beta-L-FddC); and 2',3'-dideoxy-beta-L-5-cytidine (beta-L-ddC) (col.2, lines 20-60 and col.5, structure between lines 40-50)). Schinazi discloses said compounds alone or in combination of other anti-hepatitis virus compounds provide treatment for HIV infections (col.12, lines 25-30). Schinazi discloses that said nucleoside can be combines with other anti-HBV agents such as interferon (col.3, line 35). The pharmaceutical composition of comprising the effective amount of beta-L-FddC and beta-L-ddC having a pharmaceutical acceptable carrier (col.9 to col.10, Table 1 and col.10, lines 60-67) is disclosed. Lin discloses the administration of said composition to human patients (col.10, lines 49-55). The prodrugs of said compositions are also disclosed (col.10, lines 18-20). The enantiomers of 2',3'-dideoxycytidine are disclosed

(col.3, lines 47-51). Schinazi also discloses that said nucleoside can be derivatized with a lipid (col.6, lines 5-6).

With regard to claims wherein said compounds are used against an HCV or *Flaviviridae* viral infection, the reference is silent on the use of these compounds, per se. However, the reference discloses that these compounds are useful for the treatment of HBV, HIV and other retroviruses such as HBV (abstract).

Claims 31-35, 39-42 and 46-54 are rejected under 35 U.S.C. 102(b) as being anticipated by Gagnon et al (Gagnon) (Immunopharmacology and Immunotoxicology, vol. 17, no.1, pp 17-32, 1995).

It is noted that the intended use of the instant composition for the treatment and/or prophylaxis of an HCV infection or for reducing the biological activity of a *Flaviviridae* viral infection does not have any patentable weight towards the claimed composition. Gagnon discloses 2',3'-dideoxy-beta-L5-fluorocytidine (beta-L-FddC); and 2',3'-dideoxy-beta-L-5-cytidine (beta-L-ddC) (page 20, fig.1). Gagnon discloses that these compounds for their *in vitro* toxicity in assays against human leukocyte cell lines in buffer solution (page 18, last para. and page 19).

With regard to claims wherein said compounds are used against an HCV or *Flaviviridae* viral infection, the reference is silent on the use of these compounds, per se. However, the reference discloses that these compounds are useful for the treatment of HBV, HIV and other retroviruses such as HBV (abstract).

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 31-35, 39-42 and 46-54 are rejected under 35 U.S.C. 102(b) as being anticipated by Locatelli et al (Locatelli) (J. Mol. Biol., 313, pp 683-694, 2001).

It is noted that the intended use of the instant composition for the treatment and/or prophylaxis of an HCV infection or for reducing the biological activity of a *Flaviviridae* viral infection does not have any patentable weight towards the claimed composition.

Locatelli discloses 2',3'-dideoxy-beta-L-5-cytidine (beta-L-ddC) (page 685, fig.2 wherein L-beta-ribose having X=H). Locatelli discloses that said dideoxy nucleoside has specificity to HCV (abstract). Locatelli also discloses the use of assay buffers such as Tris-HCL and MgCl2 (page 692, col.2, see Helicase and Bandshift assays).

Any inquiry concerning this communication or earlier communications from the

Examiner should be directed to Devesh Khare whose telephone number is (571)272-0653. The examiner can normally be reached on Monday to Friday from 8:00 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anna Jiang, Supervisory Patent Examiner, Art Unit 1623 can be reached at (571)272-0627. The official fax phone numbers for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published

applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Devesh Khare, Ph.D.,J.D.
Art Unit 1623

September 29, 2006